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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/044,486

01/11/2002

Roger Y. Tsien

9885

22798

7590

03/30/2007

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

P O BOX 458

ALAMEDA, CA 94501

EXAMINER

BERCH, MARK L

ART UNIT

PAPER NUMBER

1624

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/30/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/044,486

Applicant(s)

TSIEN ET AL.

Examiner

Mark L. Berch

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 17-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 17 is/are allowed.
- 6) ☒ Claim(s) 1, 18 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☒ Interview Summary (PTO-413) Paper No(s). 1/17/06.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The new wording of "Z comprises a fluorescent moiety bonded through a O, N or S atom is unclear. The term "comprises" is open-ended; it just says that some part of Z is fluorescent. Does the O/N/S have to be part of the fluorescent piece of Z or not? In other words, could Z be $-S-CH_2-(C\text{-bonded coumarin})$? Note that Z here "comprises" a fluorescent moiety, since the coumarin is present as a part of Z. Z itself is bonded through an S atom to the cephalosporin, but the coumarin itself is C-bonded. Depending on how the claim is read, this may or may not be embraced.

Claims 1 and 18 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This issue has been discussed at some length. Applicants reasoning on the linker is accepted. The linker language in the specification would not be understood as limited to linkers without only single bonds, and hence a linker linked on its left via a double bond does fall within the teaching of the specification. Accordingly the claim 17-19 language is not problematic.

However, Claims 1 and 18, unlike claim 17, permit but do not require a linker, and thus the current language reads on a circumstance where the second formula is used, but no linker is present. This is not a problem for the first formula. However, since the double bond arises purely from the linker, and the second formula does not require a linker, the second formula goes beyond what the specification describes.

The traverse is unpersuasive. Applicants first argue that paragraphs 46, 50 and 55 have the descriptive support. However, none of them provides for the second formula type with no linker.

Applicants then argue that the amendment has fixed the problem: "However, in order to expedite the application, the claim has been amended to require that the "Z" fluorophore be attached through a linker, as suggested by the Examiner." This is not true. The material after the final semicolon does provide for the linker use. But the material before that final semicolon does not have the linker, and thus the claims still read on the second formula with no linker. For example, one could have Z as an aminophthalimide, connected via its N atom in a compound of the second formula.

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Claims 1, 18, 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The specification fails to teach how to use these compounds for the scope claimed. The utility derives from the fact that the beta-lactamase enzyme cleaves a C-O bond of a phenolic ether and releases the fluorophore. See e.g. Figures 2 and 8. However, these compounds are not required to have a phenolic ether linkage, and indeed, might not even have a C-O bond of any kind. Even as claim 1 is amended, it is constructed without regard to whether or not the compound will be cleaved by a beta-lactamase.

For example, suppose that Z were a pyrene, an ordinary fluorescent moiety. Suppose the linker were carbonyl, again, a perfectly ordinary linker. Such a compound will not cleave at all. Or consider a non-linker compound, connected via a N atom, e.g. an aminophthalimide in first or second formula, linked via its exocyclic N. Beta-lactamase will not cleave that. It can cleave aromatic ethers and can cleave the β -lactam ring itself, but it cannot cleave an ordinary amine (for the first formula) or imine (for the second formula).

The traverse is unpersuasive. Applicants state, "The specification provides references and examples of functioning substrates wherein a variety of different leaving groups exist beyond phenolic leaving groups." Actually, the page 13 material consists entirely of aromatic ethers. The only exception is VIII which applicants now state was a typographical error.

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Applicants continue: "Further, a diverse range of linkers were known in the art at the time of filing that can link to "Z" groups to beta-lactams to provide functioning substrates comprising a wide variety of cleavage sites and leaving groups." To what does this refer? What art is applicant referring to?

Next, applicants state: "The original specification also provides a variety of linkers, e.g., in the paragraph 46 direct linkages and linkages through linkers containing nucleofugal O, N or S heteroatoms. These linker structures are taught as functional participants in the electron transfers described for the lactamase reaction, e.g. in paragraph 40 and provided references."

This is beside the point. The linkers are neither the problem nor the solution. It is possible that some linkers might themselves cleave, although the specification does not teach this. That is, the specification teaches the linkers only for the purpose of attaching the fluorescent donor. The actual process is cleaving off the donor itself as the phenoxide, as is seen in Figures 2 and 8.

Incidentally, the reference cited in paragraph 40 were not provided. If applicants were referring to some other references, it is not clear what these are.

Claim Objections

Claim 19 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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A handwritten signature in black ink, appearing to read "Mark L. Berch". The signature is written in a cursive, flowing style.

Mark L. Berch
Primary Examiner
Art Unit 1624

3/27/07